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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/775,554	02/09/2004	Meng Yang	312762004400	6701

25225 7590 01/22/2009

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EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	PAPER NUMBER
1633	
MAIL DATE	DELIVERY MODE
01/22/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/775,554	YANG ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *15 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,19 and 20* is/are pending in the application.

4a) Of the above claim(s) *19 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/8/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's claim amendment and response filed 7/15/08 have been entered. Claims 4-18 and 21 are canceled. Claims 1-3 and 19-20 are currently pending in the instant application. Of these, claims 19-20 remain withdrawn from prosecution as being drawn to subject matter nonelected without traverse. Claims 1-3 are therefore under consideration. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in the previous office action.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 9/8/08 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner and an initialed copy of the 1449 is attached to this action.

Claim Rejections - 35 USC § 112

The rejection of claims 1-3 and 21 under 35 U.S.C. 112, second paragraph, for indefiniteness is withdrawn in view of the cancellation of claim 21 and the amendment to claims 1-3.

The rejection of claims 1-3 and 21 under 35 U.S.C. 112, first paragraph, for new matter is withdrawn in view of the cancellation of claim 21 and the amendment to claims 1-3.

Claim Rejections - 35 USC § 102

The rejection of claims 1-3 under 35 U.S.C. 102(a) as being anticipated by WO 02/28188 A1 (4/1/02), hereafter referred to as Kern, is withdrawn in view of the amendment to claim 1 which now recites that the transgenic rodent comprises a beta actin promoter operatively linked to the nucleotide sequence encoding the fluorescent protein.

Claim Rejections - 35 USC § 103

The rejection of claims 1-3 and 21 rejected under 35 U.S.C. 103(a) as being unpatentable over WO 02/28188 A1 (4/1/02), hereafter referred to as Kern, in view of Okabe et al. (1997) FEBS Lett., Vol. 467, 313-319, is withdrawn over canceled claim 21 and maintained over amended claims 1-3. Applicant's amendments and arguments have been fully considered but have not been found persuasive in overcoming the rejection for reasons of record as discussed in detail.

The applicant argues that neither Kern et al. nor Okabe et al. individually teaches each of the elements of the invention as claimed. The applicant further argues that neither Kern et al. nor Okabe et al. teaches the specific methods steps, specifically the number of breeding crosses,

recited in the claims. According to applicants, the GFP nu/nu mice produced from the first cross, which the applicant acknowledges is taught by Kern et al., are "relatively unstable" and cannot be continuously and reliably used to breed successive generations of mice which are immunocompromised and which exhibit stable fluorescence. The applicant then argues that the claim has been amended to recite this increased stability.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Further, it is again reiterated that the claims are product by process claims. The applicant is reminded that "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

Second, the applicant is arguing limitations that are not present in the claims. The claims as written contain no limitations regarding the stability of the rodent as a final product or the stability of the rodents produced during any one of the breeding steps. It is further noted that while the applicant states that the claim has been amended to remove the optional language regarding breeding rodents obtained in the fourth crossing to reflect the stability of the rodents obtained through this more elaborate process than disclosed by Kern, there is no evidence of

record that the rodent product produced from breeding the fourth crossing is structurally different from that disclosed and suggested by Kern. As noted in the rejection of record, Kern teaches a transgenic immunodeficient organism which exhibits a detectable trait such as the expression of a detectable marker (Kern, page 4). Kern specifically teaches that the organism is a transgenic mouse, and more specifically the offspring of a nu/nu mouse, which expresses the detectable marker green fluorescent protein (Kern, page 4, and page 23, claims 18-24). Kern further teaches methods of making the mouse by stably integrating the detectable gene into the chromosome of a mouse embryonic stem cell and using the embryonic cell to develop strains of homozygous mice having two copies of the integrated construct in every cell, and then breeding the mice with nu/nu mice to produce mice that are homozygous for the transgene and homozygous for immunodeficiency (Kern, pages 10-11). Kern further teaches the constitutive expression of green fluorescent protein in the nu/nu mice (Kern, pages 13). Note in particular that Kern et al. teaches breeding the mouse transgenic for the selectable trait, such as constitutive GFP expression, to heterozygosity or homozygosity, where the transgene is integrated into the chromosomes of every cell in the mouse, and then cross-breeding that strain to a nu/nu mouse strain to create a homozygous GFP+/GFP+:nu/nu mouse or a heterozygous GFP+/-:nu/nu mouse (Kern, pages 10-11, bridging paragraph). Breeding past the first generation is a common technique and was well known at the time of filing as the only means to produce a supply of transgenic animals for experimental use. Further, Kern in fact specifically suggests at least the first two breeding steps, since the first cross would produce heterozygous mice which would then have to bred together to produce homozygous mice. The further breeding of the homozygous progeny would have been

clearly obvious to the skilled artisan based on well known breeding techniques used for decades to maintain colonies of test animals with desired genetic traits.

In addition, as noted in previous actions, Kern only differs from the instant invention by not teaching the use of the beta-actin promoter to constitutively express GFP in the immunodeficient transgenic mice. Okabe et al. was cited to supplement the teachings of Kern by teaching the production of a transgenic mouse comprising a transgene encoding GFP under control of the chicken beta-actin promoter (Okabe et al., page 313). Okabe et al. further teaches that GFP was expressed in all tissues of the mouse with the exception of erythrocytes and hair (Okabe et al., page 313). Thus, based on the specific motivation provided by Kern for breeding a transgenic mouse constitutively expressing GFP with an immunodeficient nu/nu mouse to produce a homozygous GFP+/GFP+:nu/nu mouse, and the state of the art of mouse breeding at the time of filing, it would have been *prima facie* obvious to the skilled artisan at the time of filing to breed the GFP transgenic mouse of Okabe et al., where GFP is under transcriptional control of the constitutive beta-actin promoter, with a nu/nu mouse as taught by Kern to produce an immunodeficient transgenic mouse which expresses GFP in all tissues except hair and erythrocytes. Further, based on the well developed techniques of breeding mice at the time of filing, the specific guidance provided by Kern for breeding GFP transgenic mice with nu/nu mice and the detailed guidance provided by Okabe et al. for making a transgenic mouse encoding GFP under control of a beta-actin promoter, the skilled artisan would have had a reasonable expectation of success in making an immunodeficient transgenic mouse as claimed.

Therefore, applicant's arguments are not found persuasive and the rejection of record stands.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, **the new technology center fax number is (571) 273-8300**. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

/Anne Marie S. Wehbé/
Primary Examiner, A.U. 1633